



SEQUENCE LISTING

<110> Anderson, John P.
Basi, Gurigbal
Doane, Minh Tam
Frigon, Normand
John, Varghese
Power, Michael
Sinha, Sukanto
Tatsuno, Gwen
Tung, Jay
Wang, Shuwen
McConlogue, Lisa

<120> Beta-Secretase Enzyme Compositions and
Methods

<130> 228-US-NEW2C6

<140> 09/724,569

<141> 2000-11-28

<150> US 09/501,708

<151> 2000-02-10

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<151> 1999-06-15

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| ggcaccacag | acggcatccg | gctgcccctg | cgcagcggcc | tggggggcgc | ccccctgggg | 120 |
| ctgcggctgc | cccgggagac | cgacgaagag | cccaggagag | ccggccggag | gggcagcttt | 180 |
| gtggagatgg | tggacaacct | gaggggcaag | tcggggcagg | gctactacgt | ggagatgacc | 240 |
| gtgggcagcc | ccccgcagac | gctcaacatc | ctgggtggata | caggcagcag | taactttgca | 300 |
| gtgggtgctg | ccccccaccc | cttcctgcat | cgctactacc | agaggcagct | gtccagcaca | 360 |
| taccgggacc | tccggaaggg | tgtgtatgtg | ccctacaccc | agggcaagtg | ggaaggggag | 420 |
| ctgggcaccg | acctggtaag | catcccccat | ggccccaacg | tcactgtgcg | tgccaacatt | 480 |
| gctgccatca | ctgaatcaga | caagttcttc | atcaacggct | ccaactggga | aggcatcctg | 540 |
| gggctggcct | atgctgagat | tgccaggcct | gacgactccc | tggagccttt | ctttgactct | 600 |
| ctggtaaagc | agaccacagt | tcccaacctc | ttctccctgc | agctttgtgg | tgetggcttc | 660 |
| cccccaacc | agtctgaagt | gctggcctct | gtcggaggga | gcatgatcat | tggaggtatc | 720 |
| gaccactcgc | tgtacacagg | cagtctctgg | tatacaccca | tccggcggga | gtggtattat | 780 |
| gaggtgatca | ttgtgcgggt | ggagatcaat | ggacaggatc | tgaaaatgga | ctgcaaggag | 840 |
| tacaactatg | acaagagcat | tgtggacagt | ggcaccacca | accttcgttt | gccccagaaa | 900 |
| gtgtttgaag | ctgcagtcaa | atccatcaag | gcagcctcct | ccacggagaa | gttcctgat | 960 |
| ggtttctggc | taggagagca | gctgggtgtg | tggcaagcag | gcaccacccc | ttggaacatt | 1020 |
| ttcccagtca | tctcactcta | cctaattgggt | gaggttacca | accagtcctt | ccgcatcacc | 1080 |
| atccttccgc | agcaatacct | gcggccagtg | gaagatgtgg | ccacgtccca | agacgactgt | 1140 |

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| tacaagtttg | ccatctcaca | gtcatccacg | ggcactgtta | tgggagctgt | tatcatggag | 1200 |
| ggcttctacg | ttgtctttga | tcggggcccg | aaacgaattg | gctttgctgt | cagcgcttgc | 1260 |
| catgtgcacg | atgagttcag | gacggcagcg | gtggaaggcc | cttttgtcac | cttggacatg | 1320 |
| gaagactgtg | gctacaacat | tccacagaca | gatgagtcaa | ccctcatgac | catagcctat | 1380 |
| gtcatggctg | ccatctgcgc | cctcttcatg | ctgccactct | gcctcatggg | gtgtcagtg | 1440 |
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| Met | Ala | Gln | Ala | Leu | Pro | Trp | Leu | Leu | Leu | Trp | Met | Gly | Ala | Gly | Val | 1 | 5 | 10 | 15 |
| Leu | Pro | Ala | His | Gly | Thr | Gln | His | Gly | Ile | Arg | Leu | Pro | Leu | Arg | Ser | 20 | 25 | 30 | |
| Gly | Leu | Gly | Gly | Ala | Pro | Leu | Gly | Leu | Arg | Leu | Pro | Arg | Glu | Thr | Asp | 35 | 40 | 45 | |
| Glu | Glu | Pro | Glu | Glu | Pro | Gly | Arg | Arg | Gly | Ser | Phe | Val | Glu | Met | Val | 50 | 55 | 60 | |
| Asp | Asn | Leu | Arg | Gly | Lys | Ser | Gly | Gln | Gly | Tyr | Tyr | Val | Glu | Met | Thr | 65 | 70 | 75 | 80 |
| Val | Gly | Ser | Pro | Pro | Gln | Thr | Leu | Asn | Ile | Leu | Val | Asp | Thr | Gly | Ser | 85 | 90 | 95 | |
| Ser | Asn | Phe | Ala | Val | Gly | Ala | Ala | Pro | His | Pro | Phe | Leu | His | Arg | Tyr | 100 | 105 | 110 | |
| Tyr | Gln | Arg | Gln | Leu | Ser | Ser | Thr | Tyr | Arg | Asp | Leu | Arg | Lys | Gly | Val | 115 | 120 | 125 | |
| Tyr | Val | Pro | Tyr | Thr | Gln | Gly | Lys | Trp | Glu | Gly | Glu | Leu | Gly | Thr | Asp | 130 | 135 | 140 | |
| Leu | Val | Ser | Ile | Pro | His | Gly | Pro | Asn | Val | Thr | Val | Arg | Ala | Asn | Ile | 145 | 150 | 155 | 160 |
| Ala | Ala | Ile | Thr | Glu | Ser | Asp | Lys | Phe | Phe | Ile | Asn | Gly | Ser | Asn | Trp | 165 | 170 | 175 | |
| Glu | Gly | Ile | Leu | Gly | Leu | Ala | Tyr | Ala | Glu | Ile | Ala | Arg | Pro | Asp | Asp | 180 | 185 | 190 | |
| Ser | Leu | Glu | Pro | Phe | Phe | Asp | Ser | Leu | Val | Lys | Gln | Thr | His | Val | Pro | 195 | 200 | 205 | |
| Asn | Leu | Phe | Ser | Leu | Gln | Leu | Cys | Gly | Ala | Gly | Phe | Pro | Leu | Asn | Gln | 210 | 215 | 220 | |
| Ser | Glu | Val | Leu | Ala | Ser | Val | Gly | Gly | Ser | Met | Ile | Ile | Gly | Gly | Ile | 225 | 230 | 235 | 240 |
| Asp | His | Ser | Leu | Tyr | Thr | Gly | Ser | Leu | Trp | Tyr | Thr | Pro | Ile | Arg | Arg | 245 | 250 | 255 | |
| Glu | Trp | Tyr | Tyr | Glu | Val | Ile | Ile | Val | Arg | Val | Glu | Ile | Asn | Gly | Gln | 260 | 265 | 270 | |
| Asp | Leu | Lys | Met | Asp | Cys | Lys | Glu | Tyr | Asn | Tyr | Asp | Lys | Ser | Ile | Val | 275 | 280 | 285 | |
| Asp | Ser | Gly | Thr | Thr | Asn | Leu | Arg | Leu | Pro | Lys | Lys | Val | Phe | Glu | Ala | 290 | 295 | 300 | |
| Ala | Val | Lys | Ser | Ile | Lys | Ala | Ala | Ser | Ser | Thr | Glu | Lys | Phe | Pro | Asp | 305 | 310 | 315 | 320 |
| Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val | Cys | Trp | Gln | Ala | Gly | Thr | Thr | 325 | 330 | 335 | |
| Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser | Leu | Tyr | Leu | Met | Gly | Glu | Val | 340 | 345 | 350 | |
| Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile | Leu | Pro | Gln | Gln | Tyr | Leu | Arg | 355 | 360 | 365 | |
| Pro | Val | Glu | Asp | Val | Ala | Thr | Ser | Gln | Asp | Asp | Cys | Tyr | Lys | Phe | Ala | | | | |

| | | | | |
|---|-----|-----|-----|-----|
| 370 | | 375 | | 380 |
| Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu | | | | |
| 385 | | 390 | | 400 |
| Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala | | | | |
| | 405 | | 410 | 415 |
| Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu | | | | |
| | 420 | | 425 | 430 |
| Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro | | | | |
| | 435 | | 440 | 445 |
| Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala | | | | |
| | 450 | | 455 | 460 |
| Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp | | | | |
| 465 | | 470 | | 480 |
| Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp | | | | |
| | 485 | | 490 | 495 |
| Ile Ser Leu Leu Lys | | | | |
| 500 | | | | |

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 <400> 20
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<210> 42
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 <212> DNA
 <213> Homo sapiens

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 cagacgctca acatcctggg ggatacaggc agcagtaact ttgcagtggg tgctgcccc 180
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<212> PRT
<213> Homo sapiens

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Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp
35     40     45
Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu
50     55     60
His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg
65     70     75     80
Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu
85     90     95
Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg
100    105    110
Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly
115    120    125
Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg
130    135    140
Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr
145    150    155    160
His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro
165    170    175
Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile
180    185    190
Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro
195    200    205
Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile
210    215    220

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| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Asn | Gly | Gln | Asp | Leu | Lys | Met | Asp | Cys | Lys | Glu | Tyr | Asn | Tyr | Asp | Lys |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| Ser | Ile | Val | Asp | Ser | Gly | Thr | Thr | Asn | Leu | Arg | Leu | Pro | Lys | Lys | Val |
| | | | | 245 | | | | | 250 | | | | | 255 | |
| Phe | Glu | Ala | Ala | Val | Lys | Ser | Ile | Lys | Ala | Ala | Ser | Ser | Thr | Glu | Lys |
| | | | 260 | | | | | 265 | | | | | 270 | | |
| Phe | Pro | Asp | Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val | Cys | Trp | Gln | Ala |
| | | 275 | | | | | 280 | | | | | 285 | | | |
| Gly | Thr | Thr | Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser | Leu | Tyr | Leu | Met |
| | 290 | | | | 295 | | | | | | 300 | | | | |
| Gly | Glu | Val | Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile | Leu | Pro | Gln | Gln |
| 305 | | | | 310 | | | | | | 315 | | | | | 320 |
| Tyr | Leu | Arg | Pro | Val | Glu | Asp | Val | Ala | Thr | Ser | Gln | Asp | Asp | Cys | Tyr |
| | | | 325 | | | | | 330 | | | | | | 335 | |
| Lys | Phe | Ala | Ile | Ser | Gln | Ser | Ser | Thr | Gly | Thr | Val | Met | Gly | Ala | Val |
| | | 340 | | | | | | 345 | | | | | 350 | | |
| Ile | Met | Glu | Gly | Phe | Tyr | Val | Val | Phe | Asp | Arg | Ala | Arg | Lys | Arg | Ile |
| | 355 | | | | | | 360 | | | | | 365 | | | |
| Gly | Phe | Ala | Val | Ser | Ala | Cys | His | Val | His | Asp | Glu | Phe | Arg | Thr | Ala |
| | 370 | | | | 375 | | | | | | 380 | | | | |
| Ala | Val | Glu | Gly | Pro | Phe | Val | Thr | Leu | Asp | Met | Glu | Asp | Cys | Gly | Tyr |
| 385 | | | | 390 | | | | | | 395 | | | | | 400 |
| Asn | Ile | Pro | Gln | Thr | Asp | Glu | Ser | Thr | Leu | Met | Thr | Ile | Ala | Tyr | Val |
| | | | 405 | | | | | 410 | | | | | | 415 | |
| Met | Ala | Ala | Ile | Cys | Ala | Leu | Phe | Met | Leu | Pro | Leu | Cys | Leu | Met | Val |
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| Cys | Gln | Trp | Arg | Cys | Leu | Arg | Cys | Leu | Arg | Gln | Gln | His | Asp | Asp | Phe |
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<211> 2348

<212> DNA

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| ctcccctgac | cgctctccac | agcccggacc | cgggggctgg | cccagggccc | tgcaggccct | 180 |
| ggcgtcctga | tgcccccaag | ctccctctcc | tgagaagcca | ccagcaccac | ccagacttgg | 240 |
| gggcaggcgc | cagggacgga | cgtggggccag | tgcgagccca | gaggggcccga | aggccggggc | 300 |
| ccaccatggc | ccaagccctg | ccctggctcc | tgctgtggat | gggcgcggga | gtgctgcctg | 360 |
| cccacggcac | ccagcacggc | atccggctgc | ccctgcgcag | cggcctgggg | ggcgcccccc | 420 |
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| ttgcagtggg | tgctgcccc | cacccttcc | tgcctcgcta | ctaccagagg | cagctgtcca | 660 |
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| ctgatggttt | ctggctagga | gagcagctgg | tgtgctggca | agcaggcacc | acccttgga | 1320 |
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| cctatgtcat | ggctgccatc | tgcgccctct | tcattgctgcc | actctgcctc | atgggtgtgtc | 1740 |
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| tattgactag | ttattaatag | taatcaatta | cggggtcatt | agttcatagc | ccatatatgg | 180 |
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| Gly | Leu | Gly | Gly | Ala | Pro | Leu | Gly | Leu | Arg | Leu | Pro | Arg | Glu | Thr | Asp |
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| Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val | Cys | Trp | Gln | Ala | Gly | Thr | Thr |
| | | | 325 | | | | | | 330 | | | | | 335 | |
| Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser | Leu | Tyr | Leu | Met | Gly | Glu | Val |
| | | 340 | | | | | | 345 | | | | | 350 | | |
| Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile | Leu | Pro | Gln | Gln | Tyr | Leu | Arg |
| | | 355 | | | | | 360 | | | | | 365 | | | |
| Pro | Val | Glu | Asp | Val | Ala | Thr | Ser | Gln | Asp | Asp | Cys | Tyr | Lys | Phe | Ala |
| | 370 | | | | | 375 | | | | | 380 | | | | |
| Ile | Ser | Gln | Ser | Ser | Thr | Gly | Thr | Val | Met | Gly | Ala | Val | Ile | Met | Glu |
| 385 | | | | | 390 | | | | | 395 | | | | | 400 |
| Gly | Phe | Tyr | Val | Val | Phe | Asp | Arg | Ala | Arg | Lys | Arg | Ile | Gly | Phe | Ala |
| | | | 405 | | | | | | 410 | | | | | 415 | |
| Val | Ser | Ala | | | | | | | | | | | | | |

<210> 58

<211> 407

<212> PRT

<213> Homo sapiens

<400> 58
 Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val
 1 5 10 15
 Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val
 20 25 30
 Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp
 35 40 45
 Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu
 50 55 60
 His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg
 65 70 75 80
 Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu
 85 90 95
 Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg
 100 105 110
 Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly
 115 120 125
 Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg
 130 135 140
 Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr
 145 150 155 160
 His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro
 165 170 175
 Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile
 180 185 190
 Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro
 195 200 205
 Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile
 210 215 220
 Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys
 225 230 235 240
 Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val
 245 250 255
 Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys
 260 265 270
 Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala
 275 280 285
 Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met
 290 295 300
 Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln
 305 310 315 320
 Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr
 325 330 335
 Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val
 340 345 350
 Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile
 355 360 365
 Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala
 370 375 380
 Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr
 385 390 395 400
 Asn Ile Pro Gln Thr Asp Glu
 405

<210> 59
 <211> 452
 <212> PRT
 <213> Homo sapiens

<400> 59

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Gln | Ala | Leu | Pro | Trp | Leu | Leu | Leu | Trp | Met | Gly | Ala | Gly | Val |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Leu | Pro | Ala | His | Gly | Thr | Gln | His | Gly | Ile | Arg | Leu | Pro | Leu | Arg | Ser |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Gly | Leu | Gly | Gly | Ala | Pro | Leu | Gly | Leu | Arg | Leu | Pro | Arg | Glu | Thr | Asp |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Glu | Glu | Pro | Glu | Glu | Pro | Gly | Arg | Arg | Gly | Ser | Phe | Val | Glu | Met | Val |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Asp | Asn | Leu | Arg | Gly | Lys | Ser | Gly | Gln | Gly | Tyr | Tyr | Val | Glu | Met | Thr |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| Val | Gly | Ser | Pro | Pro | Gln | Thr | Leu | Asn | Ile | Leu | Val | Asp | Thr | Gly | Ser |
| | | | | 85 | | | | | 90 | | | | | 95 | |
| Ser | Asn | Phe | Ala | Val | Gly | Ala | Ala | Pro | His | Pro | Phe | Leu | His | Arg | Tyr |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Tyr | Gln | Arg | Gln | Leu | Ser | Ser | Thr | Tyr | Arg | Asp | Leu | Arg | Lys | Gly | Val |
| | | 115 | | | | | 120 | | | | | 125 | | | |
| Tyr | Val | Pro | Tyr | Thr | Gln | Gly | Lys | Trp | Glu | Gly | Glu | Leu | Gly | Thr | Asp |
| | 130 | | | | | 135 | | | | | 140 | | | | |
| Leu | Val | Ser | Ile | Pro | His | Gly | Pro | Asn | Val | Thr | Val | Arg | Ala | Asn | Ile |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| Ala | Ala | Ile | Thr | Glu | Ser | Asp | Lys | Phe | Phe | Ile | Asn | Gly | Ser | Asn | Trp |
| | | | | 165 | | | | | 170 | | | | | 175 | |
| Glu | Gly | Ile | Leu | Gly | Leu | Ala | Tyr | Ala | Glu | Ile | Ala | Arg | Pro | Asp | Asp |
| | | | 180 | | | | | 185 | | | | 190 | | | |
| Ser | Leu | Glu | Pro | Phe | Phe | Asp | Ser | Leu | Val | Lys | Gln | Thr | His | Val | Pro |
| | 195 | | | | | | 200 | | | | | 205 | | | |
| Asn | Leu | Phe | Ser | Leu | Gln | Leu | Cys | Gly | Ala | Gly | Phe | Pro | Leu | Asn | Gln |
| | 210 | | | | 215 | | | | | | 220 | | | | |
| Ser | Glu | Val | Leu | Ala | Ser | Val | Gly | Gly | Ser | Met | Ile | Ile | Gly | Gly | Ile |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| Asp | His | Ser | Leu | Tyr | Thr | Gly | Ser | Leu | Trp | Tyr | Thr | Pro | Ile | Arg | Arg |
| | | | 245 | | | | | | 250 | | | | | 255 | |
| Glu | Trp | Tyr | Tyr | Glu | Val | Ile | Ile | Val | Arg | Val | Glu | Ile | Asn | Gly | Gln |
| | | | 260 | | | | | 265 | | | | | 270 | | |
| Asp | Leu | Lys | Met | Asp | Cys | Lys | Glu | Tyr | Asn | Tyr | Asp | Lys | Ser | Ile | Val |
| | 275 | | | | | | 280 | | | | | 285 | | | |
| Asp | Ser | Gly | Thr | Thr | Asn | Leu | Arg | Leu | Pro | Lys | Lys | Val | Phe | Glu | Ala |
| | 290 | | | | 295 | | | | | | 300 | | | | |
| Ala | Val | Lys | Ser | Ile | Lys | Ala | Ala | Ser | Ser | Thr | Glu | Lys | Phe | Pro | Asp |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val | Cys | Trp | Gln | Ala | Gly | Thr | Thr |
| | | | 325 | | | | | | 330 | | | | | 335 | |
| Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser | Leu | Tyr | Leu | Met | Gly | Glu | Val |
| | | | 340 | | | | | 345 | | | | | 350 | | |
| Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile | Leu | Pro | Gln | Gln | Tyr | Leu | Arg |
| | | 355 | | | | | 360 | | | | | 365 | | | |
| Pro | Val | Glu | Asp | Val | Ala | Thr | Ser | Gln | Asp | Asp | Cys | Tyr | Lys | Phe | Ala |
| | 370 | | | | | 375 | | | | | 380 | | | | |
| Ile | Ser | Gln | Ser | Ser | Thr | Gly | Thr | Val | Met | Gly | Ala | Val | Ile | Met | Glu |
| 385 | | | | | 390 | | | | | 395 | | | | | 400 |
| Gly | Phe | Tyr | Val | Val | Phe | Asp | Arg | Ala | Arg | Lys | Arg | Ile | Gly | Phe | Ala |
| | | | 405 | | | | | | 410 | | | | | 415 | |
| Val | Ser | Ala | Cys | His | Val | His | Asp | Glu | Phe | Arg | Thr | Ala | Ala | Val | Glu |
| | | | 420 | | | | | 425 | | | | | 430 | | |
| Gly | Pro | Phe | Val | Thr | Leu | Asp | Met | Glu | Asp | Cys | Gly | Tyr | Asn | Ile | Pro |
| | | 435 | | | | | 440 | | | | | | 445 | | |
| Gln | Thr | Asp | Glu | | | | | | | | | | | | |
| | | | 450 | | | | | | | | | | | | |

<210> 60

<211> 7
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic peptide inhibitor

 <220>
 <221> MOD_RES
 <222> 4
 <223> Xaa = hydroxyethylene

 <400> 61
 Glu Val Met Xaa Ala Glu Phe
 1 5

 <210> 62
 <211> 26
 <212> PRT
 <213> Homo sapiens

 <400> 62
 Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met
 1 5 10 15
 Leu Pro Leu Cys Leu Met Val Cys Gln Trp
 20 25

 <210> 63
 <211> 33
 <212> PRT
 <213> Homo sapiens

 <220>
 <223> P26-P4'sw peptide substrate

 <400> 63
 Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu
 1 5 10 15
 Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu
 20 25 30
 Phe

 <210> 64
 <211> 29
 <212> PRT
 <213> Homo sapiens

 <220>
 <223> P26-P1' peptide substrate with CGG linker

 <400> 64
 Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu
 1 5 10 15
 Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu
 20 25

 <210> 65
 <211> 501
 <212> PRT
 <213> Mus musculus

<400> 65

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Pro | Ala | Leu | His | Trp | Leu | Leu | Leu | Trp | Val | Gly | Ser | Gly | Met |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Leu | Pro | Ala | Gln | Gly | Thr | His | Leu | Gly | Ile | Arg | Leu | Pro | Leu | Arg | Ser |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Gly | Leu | Ala | Gly | Pro | Pro | Leu | Gly | Leu | Arg | Leu | Pro | Arg | Glu | Thr | Asp |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Glu | Glu | Ser | Glu | Glu | Pro | Gly | Arg | Arg | Gly | Ser | Phe | Val | Glu | Met | Val |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Asp | Asn | Leu | Arg | Gly | Lys | Ser | Gly | Gln | Gly | Tyr | Tyr | Val | Glu | Met | Thr |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| Val | Gly | Ser | Pro | Pro | Gln | Thr | Leu | Asn | Ile | Leu | Val | Asp | Thr | Gly | Ser |
| | | | | 85 | | | | | 90 | | | | | 95 | |
| Ser | Asn | Phe | Ala | Val | Gly | Ala | Ala | Pro | His | Pro | Phe | Leu | His | Arg | Tyr |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Tyr | Gln | Arg | Gln | Leu | Ser | Ser | Thr | Tyr | Arg | Asp | Leu | Arg | Lys | Gly | Val |
| | 115 | | | | | | 120 | | | | | 125 | | | |
| Tyr | Val | Pro | Tyr | Thr | Gln | Gly | Lys | Trp | Glu | Gly | Glu | Leu | Gly | Thr | Asp |
| | 130 | | | | | 135 | | | | | 140 | | | | |
| Leu | Val | Ser | Ile | Pro | His | Gly | Pro | Asn | Val | Thr | Val | Arg | Ala | Asn | Ile |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| Ala | Ala | Ile | Thr | Glu | Ser | Asp | Lys | Phe | Phe | Ile | Asn | Gly | Ser | Asn | Trp |
| | | | | 165 | | | | | 170 | | | | | 175 | |
| Glu | Gly | Ile | Leu | Gly | Leu | Ala | Tyr | Ala | Glu | Ile | Ala | Arg | Pro | Asp | Asp |
| | | | 180 | | | | 185 | | | | | | 190 | | |
| Ser | Leu | Glu | Pro | Phe | Phe | Asp | Ser | Leu | Val | Lys | Gln | Thr | His | Ile | Pro |
| | 195 | | | | | 200 | | | | | 205 | | | | |
| Asn | Ile | Phe | Ser | Leu | Gln | Leu | Cys | Gly | Ala | Gly | Phe | Pro | Leu | Asn | Gln |
| | 210 | | | | 215 | | | | | | 220 | | | | |
| Thr | Glu | Ala | Leu | Ala | Ser | Val | Gly | Gly | Ser | Met | Ile | Ile | Gly | Gly | Ile |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| Asp | His | Ser | Leu | Tyr | Thr | Gly | Ser | Leu | Trp | Tyr | Thr | Pro | Ile | Arg | Arg |
| | | | 245 | | | | | | 250 | | | | | 255 | |
| Glu | Trp | Tyr | Tyr | Glu | Val | Ile | Ile | Val | Arg | Val | Glu | Ile | Asn | Gly | Gln |
| | | | 260 | | | | | 265 | | | | | 270 | | |
| Asp | Leu | Lys | Met | Asp | Cys | Lys | Glu | Tyr | Asn | Tyr | Asp | Lys | Ser | Ile | Val |
| | 275 | | | | | | 280 | | | | | 285 | | | |
| Asp | Ser | Gly | Thr | Thr | Asn | Leu | Arg | Leu | Pro | Lys | Lys | Val | Phe | Glu | Ala |
| | 290 | | | | 295 | | | | | | 300 | | | | |
| Ala | Val | Lys | Ser | Ile | Lys | Ala | Ala | Ser | Ser | Thr | Glu | Lys | Phe | Pro | Asp |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val | Cys | Trp | Gln | Ala | Gly | Thr | Thr |
| | | | 325 | | | | | 330 | | | | | | 335 | |
| Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser | Leu | Tyr | Leu | Met | Gly | Glu | Val |
| | | | 340 | | | | | 345 | | | | | 350 | | |
| Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile | Leu | Pro | Gln | Gln | Tyr | Leu | Arg |
| | 355 | | | | | | 360 | | | | | 365 | | | |
| Pro | Val | Glu | Asp | Val | Ala | Thr | Ser | Gln | Asp | Asp | Cys | Tyr | Lys | Phe | Ala |
| | 370 | | | | 375 | | | | | | 380 | | | | |
| Val | Ser | Gln | Ser | Ser | Thr | Gly | Thr | Val | Met | Gly | Ala | Val | Ile | Met | Glu |
| 385 | | | | | 390 | | | | | 395 | | | | | 400 |
| Gly | Phe | Tyr | Val | Val | Phe | Asp | Arg | Ala | Arg | Lys | Arg | Ile | Gly | Phe | Ala |
| | | | 405 | | | | | 410 | | | | | | 415 | |
| Val | Ser | Ala | Cys | His | Val | His | Asp | Glu | Phe | Arg | Thr | Ala | Ala | Val | Glu |
| | | | 420 | | | | | 425 | | | | | 430 | | |
| Gly | Pro | Phe | Val | Thr | Ala | Asp | Met | Glu | Asp | Cys | Gly | Tyr | Asn | Ile | Pro |
| | 435 | | | | | 440 | | | | | 445 | | | | |
| Gln | Thr | Asp | Glu | Ser | Thr | Leu | Met | Thr | Ile | Ala | Tyr | Val | Met | Ala | Ala |
| | 450 | | | | | 455 | | | | | 460 | | | | |
| Ile | Cys | Ala | Leu | Phe | Met | Leu | Pro | Leu | Cys | Leu | Met | Val | Cys | Gln | Trp |

465 470 475 480
 Arg Cys Leu Arg Cys Leu Arg His Gln His Asp Asp Phe Gly Asp Asp
 485 490 495
 Ile Ser Leu Leu Lys
 500

<210> 66
 <211> 480
 <212> PRT
 <213> Homo sapiens

<400> 66
 Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly Ala
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 Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu
 20 25 30
 Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly
 35 40 45
 Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro
 50 55 60
 Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val
 65 70 75 80
 Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu
 85 90 95
 Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr
 100 105 110
 Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro
 115 120 125
 His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu
 130 135 140
 Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly
 145 150 155 160
 Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe
 165 170 175
 Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu
 180 185 190
 Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala
 195 200 205
 Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr
 210 215 220
 Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu
 225 230 235 240
 Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp
 245 250 255
 Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr
 260 265 270
 Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile
 275 280 285
 Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly
 290 295 300
 Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe
 305 310 315 320
 Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe
 325 330 335
 Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val
 340 345 350
 Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser
 355 360 365
 Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val
 370 375 380
 Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 385 | | | | | 390 | | | | | 395 | | | | | 400 |
| Val | His | Asp | Glu | Phe | Arg | Thr | Ala | Ala | Val | Glu | Gly | Pro | Phe | Val | Thr |
| | | | | 405 | | | | | 410 | | | | | 415 | |
| Leu | Asp | Met | Glu | Asp | Cys | Gly | Tyr | Asn | Ile | Pro | Gln | Thr | Asp | Glu | Ser |
| | | | 420 | | | | | 425 | | | | | 430 | | |
| Thr | Leu | Met | Thr | Ile | Ala | Tyr | Val | Met | Ala | Ala | Ile | Cys | Ala | Leu | Phe |
| | | 435 | | | | | 440 | | | | | 445 | | | |
| Met | Leu | Pro | Leu | Cys | Leu | Met | Val | Cys | Gln | Trp | Arg | Cys | Leu | Arg | Cys |
| | 450 | | | | | 455 | | | | | 460 | | | | |
| Leu | Arg | Gln | Gln | His | Asp | Asp | Phe | Ala | Asp | Asp | Ile | Ser | Leu | Leu | Lys |
| 465 | | | | | 470 | | | | | 475 | | | | | 480 |

<210> 67

<211> 444

<212> PRT

<213> Homo sapiens

<400> 67

| | | | | | | | | | | | | | | | |
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| Gly | Ser | Phe | Val | Glu | Met | Val | Asp | Asn | Leu | Arg | Gly | Lys | Ser | Gly | Gln |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |
| Gly | Tyr | Tyr | Val | Glu | Met | Thr | Val | Gly | Ser | Pro | Pro | Gln | Thr | Leu | Asn |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Ile | Leu | Val | Asp | Thr | Gly | Ser | Ser | Asn | Phe | Ala | Val | Gly | Ala | Ala | Pro |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| His | Pro | Phe | Leu | His | Arg | Tyr | Tyr | Gln | Arg | Gln | Leu | Ser | Ser | Thr | Tyr |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Arg | Asp | Leu | Arg | Lys | Gly | Val | Tyr | Val | Pro | Tyr | Thr | Gln | Gly | Lys | Trp |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 |
| Glu | Gly | Glu | Leu | Gly | Thr | Asp | Leu | Val | Ser | Ile | Pro | His | Gly | Pro | Asn |
| | | | | 85 | | | | | 90 | | | | | 95 | |
| Val | Thr | Val | Arg | Ala | Asn | Ile | Ala | Ala | Ile | Thr | Glu | Ser | Asp | Lys | Phe |
| | | | 100 | | | | 105 | | | | | | 110 | | |
| Phe | Ile | Asn | Gly | Ser | Asn | Trp | Glu | Gly | Ile | Leu | Gly | Leu | Ala | Tyr | Ala |
| | | 115 | | | | | 120 | | | | | 125 | | | |
| Glu | Ile | Ala | Arg | Pro | Asp | Asp | Ser | Leu | Glu | Pro | Phe | Phe | Asp | Ser | Leu |
| | 130 | | | | 135 | | | | | | 140 | | | | |
| Val | Lys | Gln | Thr | His | Val | Pro | Asn | Leu | Phe | Ser | Leu | Gln | Leu | Cys | Gly |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| Ala | Gly | Phe | Pro | Leu | Asn | Gln | Ser | Glu | Val | Leu | Ala | Ser | Val | Gly | Gly |
| | | | | 165 | | | | | 170 | | | | | 175 | |
| Ser | Met | Ile | Ile | Gly | Gly | Ile | Asp | His | Ser | Leu | Tyr | Thr | Gly | Ser | Leu |
| | | 180 | | | | | | 185 | | | | | 190 | | |
| Trp | Tyr | Thr | Pro | Ile | Arg | Arg | Glu | Trp | Tyr | Tyr | Glu | Val | Ile | Ile | Val |
| | 195 | | | | | | 200 | | | | | 205 | | | |
| Arg | Val | Glu | Ile | Asn | Gly | Gln | Asp | Leu | Lys | Met | Asp | Cys | Lys | Glu | Tyr |
| | 210 | | | | 215 | | | | | | 220 | | | | |
| Asn | Tyr | Asp | Lys | Ser | Ile | Val | Asp | Ser | Gly | Thr | Thr | Asn | Leu | Arg | Leu |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| Pro | Lys | Lys | Val | Phe | Glu | Ala | Ala | Val | Lys | Ser | Ile | Lys | Ala | Ala | Ser |
| | | | | 245 | | | | | 250 | | | | | 255 | |
| Ser | Thr | Glu | Lys | Phe | Pro | Asp | Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val |
| | | 260 | | | | | | 265 | | | | | 270 | | |
| Cys | Trp | Gln | Ala | Gly | Thr | Thr | Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser |
| | 275 | | | | | | 280 | | | | | 285 | | | |
| Leu | Tyr | Leu | Met | Gly | Glu | Val | Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile |
| | 290 | | | | | 295 | | | | | 300 | | | | |
| Leu | Pro | Gln | Gln | Tyr | Leu | Arg | Pro | Val | Glu | Asp | Val | Ala | Thr | Ser | Gln |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| Asp | Asp | Cys | Tyr | Lys | Phe | Ala | Ile | Ser | Gln | Ser | Ser | Thr | Gly | Thr | Val |
| | | | | 325 | | | | | 330 | | | | | 335 | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|
| Met | Gly | Ala | Val | Ile | Met | Glu | Gly | Phe | Tyr | Val | Val | Phe | Asp | Arg | Ala | | |
| | | | 340 | | | | | 345 | | | | | 350 | | | | |
| Arg | Lys | Arg | Ile | Gly | Phe | Ala | Val | Ser | Ala | Cys | His | Val | His | Asp | Glu | | |
| | | 355 | | | | | 360 | | | | | 365 | | | | | |
| Phe | Arg | Thr | Ala | Ala | Val | Glu | Gly | Pro | Phe | Val | Thr | Leu | Asp | Met | Glu | | |
| | | 370 | | | | 375 | | | | | 380 | | | | | | |
| Asp | Cys | Gly | Tyr | Asn | Ile | Pro | Gln | Thr | Asp | Glu | Ser | Thr | Leu | Met | Thr | | |
| 385 | | | | | 390 | | | | | 395 | | | | | 400 | | |
| Ile | Ala | Tyr | Val | Met | Ala | Ala | Ile | Cys | Ala | Leu | Phe | Met | Leu | Pro | Leu | | |
| | | | | | | | | | | | | | | | | | |
| | | | | 405 | | | | 410 | | | | | | 415 | | | |
| Cys | Leu | Met | Val | Cys | Gln | Trp | Arg | Cys | Leu | Arg | Cys | Leu | Arg | Gln | Gln | | |
| | | | 420 | | | | | 425 | | | | | 430 | | | | |
| His | Asp | Asp | Phe | Ala | Asp | Asp | Ile | Ser | Leu | Leu | Lys | | | | | | |
| | | 435 | | | | | 440 | | | | | | | | | | |

<210> 68

<211> 395

<212> PRT

<213> Homo sapiens

<400> 68

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| Gly | Ser | Phe | Val | Glu | Met | Val | Asp | Asn | Leu | Arg | Gly | Lys | Ser | Gly | Gln | | |
| 1 | | | | 5 | | | | 10 | | | | | | 15 | | | |
| Gly | Tyr | Tyr | Val | Glu | Met | Thr | Val | Gly | Ser | Pro | Pro | Gln | Thr | Leu | Asn | | |
| | | | 20 | | | | | 25 | | | | 30 | | | | | |
| Ile | Leu | Val | Asp | Thr | Gly | Ser | Ser | Asn | Phe | Ala | Val | Gly | Ala | Ala | Pro | | |
| | | 35 | | | | 40 | | | | | | 45 | | | | | |
| His | Pro | Phe | Leu | His | Arg | Tyr | Gln | Arg | Gln | Leu | Ser | Ser | Thr | Tyr | | | |
| | 50 | | | | | 55 | | | | 60 | | | | | | | |
| Arg | Asp | Leu | Arg | Lys | Gly | Val | Tyr | Val | Pro | Tyr | Thr | Gln | Gly | Lys | Trp | | |
| 65 | | | | 70 | | | | | 75 | | | | | 80 | | | |
| Glu | Gly | Glu | Leu | Gly | Thr | Asp | Leu | Val | Ser | Ile | Pro | His | Gly | Pro | Asn | | |
| | | | 85 | | | | | 90 | | | | | 95 | | | | |
| Val | Thr | Val | Arg | Ala | Asn | Ile | Ala | Ala | Ile | Thr | Glu | Ser | Asp | Lys | Phe | | |
| | | | 100 | | | | 105 | | | | | | 110 | | | | |
| Phe | Ile | Asn | Gly | Ser | Asn | Trp | Glu | Gly | Ile | Leu | Gly | Leu | Ala | Tyr | Ala | | |
| | | 115 | | | | 120 | | | | | | 125 | | | | | |
| Glu | Ile | Ala | Arg | Pro | Asp | Asp | Ser | Leu | Glu | Pro | Phe | Phe | Asp | Ser | Leu | | |
| | 130 | | | | 135 | | | | | | 140 | | | | | | |
| Val | Lys | Gln | Thr | His | Val | Pro | Asn | Leu | Phe | Ser | Leu | Gln | Leu | Cys | Gly | | |
| 145 | | | | 150 | | | | | 155 | | | | | 160 | | | |
| Ala | Gly | Phe | Pro | Leu | Asn | Gln | Ser | Glu | Val | Leu | Ala | Ser | Val | Gly | Gly | | |
| | | | 165 | | | | | 170 | | | | | | 175 | | | |
| Ser | Met | Ile | Ile | Gly | Gly | Ile | Asp | His | Ser | Leu | Tyr | Thr | Gly | Ser | Leu | | |
| | | 180 | | | | | 185 | | | | | | 190 | | | | |
| Trp | Tyr | Thr | Pro | Ile | Arg | Arg | Glu | Trp | Tyr | Tyr | Glu | Val | Ile | Ile | Val | | |
| | | 195 | | | | | 200 | | | | | 205 | | | | | |
| Arg | Val | Glu | Ile | Asn | Gly | Gln | Asp | Leu | Lys | Met | Asp | Cys | Lys | Glu | Tyr | | |
| | 210 | | | | 215 | | | | | | 220 | | | | | | |
| Asn | Tyr | Asp | Lys | Ser | Ile | Val | Asp | Ser | Gly | Thr | Thr | Asn | Leu | Arg | Leu | | |
| 225 | | | | 230 | | | | | 235 | | | | | 240 | | | |
| Pro | Lys | Lys | Val | Phe | Glu | Ala | Ala | Val | Lys | Ser | Ile | Lys | Ala | Ala | Ser | | |
| | | | 245 | | | | | 250 | | | | | 255 | | | | |
| Ser | Thr | Glu | Lys | Phe | Pro | Asp | Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val | | |
| | | 260 | | | | | 265 | | | | | 270 | | | | | |
| Cys | Trp | Gln | Ala | Gly | Thr | Thr | Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser | | |
| | 275 | | | | | | 280 | | | | | 285 | | | | | |
| Leu | Tyr | Leu | Met | Gly | Glu | Val | Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile | | |
| | 290 | | | | 295 | | | | 300 | | | | | | | | |
| Leu | Pro | Gln | Gln | Tyr | Leu | Arg | Pro | Val | Glu | Asp | Val | Ala | Thr | Ser | Gln | | |

| | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 305 | | | | | 310 | | | | | 315 | | | | 320 |
| Asp | Asp | Cys | Tyr | Lys | Phe | Ala | Ile | Ser | Gln | Ser | Ser | Thr | Gly | Thr |
| | | | | 325 | | | | | 330 | | | | | 335 |
| Met | Gly | Ala | Val | Ile | Met | Glu | Gly | Phe | Tyr | Val | Val | Phe | Asp | Arg |
| | | | 340 | | | | | 345 | | | | | 350 | |
| Arg | Lys | Arg | Ile | Gly | Phe | Ala | Val | Ser | Ala | Cys | His | Val | His | Asp |
| | 355 | | | | | | 360 | | | | | 365 | | Glu |
| Phe | Arg | Thr | Ala | Ala | Val | Glu | Gly | Pro | Phe | Val | Thr | Leu | Asp | Met |
| | 370 | | | | | 375 | | | | | 380 | | | Glu |
| Asp | Cys | Gly | Tyr | Asn | Ile | Pro | Gln | Thr | Asp | Glu | | | | |
| 385 | | | | | 390 | | | | | 395 | | | | |

<210> 69

<211> 439

<212> PRT

<213> Homo sapiens

<400> 69

| | | | | | | | | | | | | | | | |
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| Met | Val | Asp | Asn | Leu | Arg | Gly | Lys | Ser | Gly | Gln | Gly | Tyr | Tyr | Val | Glu |
| 1 | | | 5 | | | | | | 10 | | | | | 15 | |
| Met | Thr | Val | Gly | Ser | Pro | Pro | Gln | Thr | Leu | Asn | Ile | Leu | Val | Asp | Thr |
| | | | 20 | | | | | 25 | | | | | 30 | | |
| Gly | Ser | Ser | Asn | Phe | Ala | Val | Gly | Ala | Ala | Pro | His | Pro | Phe | Leu | His |
| | | 35 | | | | | 40 | | | | | 45 | | | |
| Arg | Tyr | Tyr | Gln | Arg | Gln | Leu | Ser | Ser | Thr | Tyr | Arg | Asp | Leu | Arg | Lys |
| | 50 | | | | | 55 | | | | | 60 | | | | |
| Gly | Val | Tyr | Val | Pro | Tyr | Thr | Gln | Gly | Lys | Trp | Glu | Gly | Glu | Leu | Gly |
| 65 | | | | | 70 | | | | | 75 | | | | 80 | |
| Thr | Asp | Leu | Val | Ser | Ile | Pro | His | Gly | Pro | Asn | Val | Thr | Val | Arg | Ala |
| | | | | 85 | | | | | 90 | | | | | 95 | |
| Asn | Ile | Ala | Ala | Ile | Thr | Glu | Ser | Asp | Lys | Phe | Phe | Ile | Asn | Gly | Ser |
| | | | 100 | | | | | 105 | | | | | 110 | | |
| Asn | Trp | Glu | Gly | Ile | Leu | Gly | Leu | Ala | Tyr | Ala | Glu | Ile | Ala | Arg | Pro |
| | | 115 | | | | | 120 | | | | | | 125 | | |
| Asp | Asp | Ser | Leu | Glu | Pro | Phe | Phe | Asp | Ser | Leu | Val | Lys | Gln | Thr | His |
| | 130 | | | | | 135 | | | | | 140 | | | | |
| Val | Pro | Asn | Leu | Phe | Ser | Leu | Gln | Leu | Cys | Gly | Ala | Gly | Phe | Pro | Leu |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| Asn | Gln | Ser | Glu | Val | Leu | Ala | Ser | Val | Gly | Gly | Ser | Met | Ile | Ile | Gly |
| | | | | 165 | | | | | 170 | | | | | 175 | |
| Gly | Ile | Asp | His | Ser | Leu | Tyr | Thr | Gly | Ser | Leu | Trp | Tyr | Thr | Pro | Ile |
| | | | 180 | | | | | 185 | | | | | 190 | | |
| Arg | Arg | Glu | Trp | Tyr | Tyr | Glu | Val | Ile | Ile | Val | Arg | Val | Glu | Ile | Asn |
| | | 195 | | | | | 200 | | | | | 205 | | | |
| Gly | Gln | Asp | Leu | Lys | Met | Asp | Cys | Lys | Glu | Tyr | Asn | Tyr | Asp | Lys | Ser |
| | 210 | | | | | 215 | | | | | 220 | | | | |
| Ile | Val | Asp | Ser | Gly | Thr | Thr | Asn | Leu | Arg | Leu | Pro | Lys | Lys | Val | Phe |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| Glu | Ala | Ala | Val | Lys | Ser | Ile | Lys | Ala | Ala | Ser | Ser | Thr | Glu | Lys | Phe |
| | | | | 245 | | | | | 250 | | | | | 255 | |
| Pro | Asp | Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val | Cys | Trp | Gln | Ala | Gly |
| | | | 260 | | | | | 265 | | | | | 270 | | |
| Thr | Thr | Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser | Leu | Tyr | Leu | Met | Gly |
| | | 275 | | | | | 280 | | | | | 285 | | | |
| Glu | Val | Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile | Leu | Pro | Gln | Gln | Tyr |
| | 290 | | | | | 295 | | | | | 300 | | | | |
| Leu | Arg | Pro | Val | Glu | Asp | Val | Ala | Thr | Ser | Gln | Asp | Asp | Cys | Tyr | Lys |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| Phe | Ala | Ile | Ser | Gln | Ser | Ser | Thr | Gly | Thr | Val | Met | Gly | Ala | Val | Ile |
| | | | | 325 | | | | | 330 | | | | | 335 | |
| Met | Glu | Gly | Phe | Tyr | Val | Val | Phe | Asp | Arg | Ala | Arg | Lys | Arg | Ile | Gly |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| | | | 340 | | | | | 345 | | | | | 350 | | | |
| Phe | Ala | Val | Ser | Ala | Cys | His | Val | His | Asp | Glu | Phe | Arg | Thr | Ala | Ala | |
| | | | 355 | | | | | 360 | | | | | 365 | | | |
| Val | Glu | Gly | Pro | Phe | Val | Thr | Leu | Asp | Met | Glu | Asp | Cys | Gly | Tyr | Asn | |
| | | | 370 | | | | 375 | | | | | | 380 | | | |
| Ile | Pro | Gln | Thr | Asp | Glu | Ser | Thr | Leu | Met | Thr | Ile | Ala | Tyr | Val | Met | |
| 385 | | | | | | 390 | | | | | 395 | | | | 400 | |
| Ala | Ala | Ile | Cys | Ala | Leu | Phe | Met | Leu | Pro | Leu | Cys | Leu | Met | Val | Cys | |
| | | | | 405 | | | | | 410 | | | | | | 415 | |
| Gln | Trp | Arg | Cys | Leu | Arg | Cys | Leu | Arg | Gln | Gln | His | Asp | Asp | Phe | Ala | |
| | | | 420 | | | | | 425 | | | | | | 430 | | |
| Asp | Asp | Ile | Ser | Leu | Leu | Lys | | | | | | | | | | |
| | | | 435 | | | | | | | | | | | | | |

<210> 70
 <211> 390
 <212> PRT
 <213> Homo sapiens

<400> 70

| | | | | | | | | | | | | | | | | |
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| Met | Val | Asp | Asn | Leu | Arg | Gly | Lys | Ser | Gly | Gln | Gly | Tyr | Tyr | Val | Glu | |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | | |
| Met | Thr | Val | Gly | Ser | Pro | Pro | Gln | Thr | Leu | Asn | Ile | Leu | Val | Asp | Thr | |
| | | | 20 | | | | | 25 | | | | | 30 | | | |
| Gly | Ser | Ser | Asn | Phe | Ala | Val | Gly | Ala | Ala | Pro | His | Pro | Phe | Leu | His | |
| | | | 35 | | | | 40 | | | | | 45 | | | | |
| Arg | Tyr | Tyr | Gln | Arg | Gln | Leu | Ser | Ser | Thr | Tyr | Arg | Asp | Leu | Arg | Lys | |
| | 50 | | | | | 55 | | | | | 60 | | | | | |
| Gly | Val | Tyr | Val | Pro | Tyr | Thr | Gln | Gly | Lys | Trp | Glu | Gly | Glu | Leu | Gly | |
| 65 | | | | | 70 | | | | | 75 | | | | 80 | | |
| Thr | Asp | Leu | Val | Ser | Ile | Pro | His | Gly | Pro | Asn | Val | Thr | Val | Arg | Ala | |
| | | | | 85 | | | | | 90 | | | | | 95 | | |
| Asn | Ile | Ala | Ala | Ile | Thr | Glu | Ser | Asp | Lys | Phe | Phe | Ile | Asn | Gly | Ser | |
| | | | 100 | | | | | 105 | | | | | 110 | | | |
| Asn | Trp | Glu | Gly | Ile | Leu | Gly | Leu | Ala | Tyr | Ala | Glu | Ile | Ala | Arg | Pro | |
| | | 115 | | | | 120 | | | | | | 125 | | | | |
| Asp | Asp | Ser | Leu | Glu | Pro | Phe | Asp | Ser | Leu | Val | Lys | Gln | Thr | His | | |
| | 130 | | | | | 135 | | | | | 140 | | | | | |
| Val | Pro | Asn | Leu | Phe | Ser | Leu | Gln | Leu | Cys | Gly | Ala | Gly | Phe | Pro | Leu | |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 | |
| Asn | Gln | Ser | Glu | Val | Leu | Ala | Ser | Val | Gly | Gly | Ser | Met | Ile | Ile | Gly | |
| | | | | 165 | | | | | 170 | | | | | 175 | | |
| Gly | Ile | Asp | His | Ser | Leu | Tyr | Thr | Gly | Ser | Leu | Trp | Tyr | Thr | Pro | Ile | |
| | | | 180 | | | | | 185 | | | | | | 190 | | |
| Arg | Arg | Glu | Trp | Tyr | Tyr | Glu | Val | Ile | Ile | Val | Arg | Val | Glu | Ile | Asn | |
| | | 195 | | | | | 200 | | | | | 205 | | | | |
| Gly | Gln | Asp | Leu | Lys | Met | Asp | Cys | Lys | Glu | Tyr | Asn | Tyr | Asp | Lys | Ser | |
| | | 210 | | | | 215 | | | | | | 220 | | | | |
| Ile | Val | Asp | Ser | Gly | Thr | Thr | Asn | Leu | Arg | Leu | Pro | Lys | Lys | Val | Phe | |
| 225 | | | | | 230 | | | | | | 235 | | | | 240 | |
| Glu | Ala | Ala | Val | Lys | Ser | Ile | Lys | Ala | Ala | Ser | Ser | Thr | Glu | Lys | Phe | |
| | | | | 245 | | | | | 250 | | | | | 255 | | |
| Pro | Asp | Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val | Cys | Trp | Gln | Ala | Gly | |
| | | | 260 | | | | | 265 | | | | | | 270 | | |
| Thr | Thr | Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser | Leu | Tyr | Leu | Met | Gly | |
| | | | 275 | | | | 280 | | | | | | 285 | | | |
| Glu | Val | Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile | Leu | Pro | Gln | Gln | Tyr | |
| | 290 | | | | | 295 | | | | | 300 | | | | | |
| Leu | Arg | Pro | Val | Glu | Asp | Val | Ala | Thr | Ser | Gln | Asp | Asp | Cys | Tyr | Lys | |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 | |
| Phe | Ala | Ile | Ser | Gln | Ser | Ser | Thr | Gly | Thr | Val | Met | Gly | Ala | Val | Ile | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| | | | | 325 | | | | | 330 | | | | | 335 | | |
| Met | Glu | Gly | Phe | Tyr | Val | Val | Phe | Asp | Arg | Ala | Arg | Lys | Arg | Ile | Gly | |
| | | | 340 | | | | | 345 | | | | | 350 | | | |
| Phe | Ala | Val | Ser | Ala | Cys | His | Val | His | Asp | Glu | Phe | Arg | Thr | Ala | Ala | |
| | | 355 | | | | | 360 | | | | | 365 | | | | |
| Val | Glu | Gly | Pro | Phe | Val | Thr | Leu | Asp | Met | Glu | Asp | Cys | Gly | Tyr | Asn | |
| | 370 | | | | | 375 | | | | | 380 | | | | | |
| Ile | Pro | Gln | Thr | Asp | Glu | | | | | | | | | | | |
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<210> 71

<211> 374

<212> PRT

<213> Homo sapiens

<400> 71

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| Glu | Thr | Asp | Glu | Glu | Pro | Glu | Glu | Pro | Gly | Arg | Arg | Gly | Ser | Phe | Val | |
| 1 | | | 5 | | | | | | 10 | | | | | 15 | | |
| Glu | Met | Val | Asp | Asn | Leu | Arg | Gly | Lys | Ser | Gly | Gln | Gly | Tyr | Tyr | Val | |
| | | 20 | | | | | | 25 | | | | | 30 | | | |
| Glu | Met | Thr | Val | Gly | Ser | Pro | Pro | Gln | Thr | Leu | Asn | Ile | Leu | Val | Asp | |
| | | 35 | | | | | 40 | | | | | 45 | | | | |
| Thr | Gly | Ser | Ser | Asn | Phe | Ala | Val | Gly | Ala | Ala | Pro | His | Pro | Phe | Leu | |
| | 50 | | | | 55 | | | | | | 60 | | | | | |
| His | Arg | Tyr | Tyr | Gln | Arg | Gln | Leu | Ser | Ser | Thr | Tyr | Arg | Asp | Leu | Arg | |
| 65 | | | | 70 | | | | | | 75 | | | | | 80 | |
| Lys | Gly | Val | Tyr | Val | Pro | Tyr | Thr | Gln | Gly | Lys | Trp | Glu | Gly | Glu | Leu | |
| | | | 85 | | | | | | 90 | | | | | 95 | | |
| Gly | Thr | Asp | Leu | Val | Ser | Ile | Pro | His | Gly | Pro | Asn | Val | Thr | Val | Arg | |
| | | 100 | | | | | | 105 | | | | | 110 | | | |
| Ala | Asn | Ile | Ala | Ala | Ile | Thr | Glu | Ser | Asp | Lys | Phe | Phe | Ile | Asn | Gly | |
| | | 115 | | | | | 120 | | | | | 125 | | | | |
| Ser | Asn | Trp | Glu | Gly | Ile | Leu | Gly | Leu | Ala | Tyr | Ala | Glu | Ile | Ala | Arg | |
| | 130 | | | | | 135 | | | | | 140 | | | | | |
| Pro | Asp | Asp | Ser | Leu | Glu | Pro | Phe | Phe | Asp | Ser | Leu | Val | Lys | Gln | Thr | |
| 145 | | | | 150 | | | | | | 155 | | | | | 160 | |
| His | Val | Pro | Asn | Leu | Phe | Ser | Leu | Gln | Leu | Cys | Gly | Ala | Gly | Phe | Pro | |
| | | | 165 | | | | | | 170 | | | | | 175 | | |
| Leu | Asn | Gln | Ser | Glu | Val | Leu | Ala | Ser | Val | Gly | Gly | Ser | Met | Ile | Ile | |
| | | 180 | | | | | | 185 | | | | | 190 | | | |
| Gly | Gly | Ile | Asp | His | Ser | Leu | Tyr | Thr | Gly | Ser | Leu | Trp | Tyr | Thr | Pro | |
| | | 195 | | | | | 200 | | | | | 205 | | | | |
| Ile | Arg | Arg | Glu | Trp | Tyr | Tyr | Glu | Val | Ile | Ile | Val | Arg | Val | Glu | Ile | |
| | 210 | | | | 215 | | | | | | 220 | | | | | |
| Asn | Gly | Gln | Asp | Leu | Lys | Met | Asp | Cys | Lys | Glu | Tyr | Asn | Tyr | Asp | Lys | |
| 225 | | | | 230 | | | | | | 235 | | | | | 240 | |
| Ser | Ile | Val | Asp | Ser | Gly | Thr | Thr | Asn | Leu | Arg | Leu | Pro | Lys | Lys | Val | |
| | | | 245 | | | | | | 250 | | | | | 255 | | |
| Phe | Glu | Ala | Ala | Val | Lys | Ser | Ile | Lys | Ala | Ala | Ser | Ser | Thr | Glu | Lys | |
| | | 260 | | | | | | 265 | | | | | 270 | | | |
| Phe | Pro | Asp | Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val | Cys | Trp | Gln | Ala | |
| | | 275 | | | | | 280 | | | | | 285 | | | | |
| Gly | Thr | Thr | Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser | Leu | Tyr | Leu | Met | |
| | 290 | | | | 295 | | | | | | 300 | | | | | |
| Gly | Glu | Val | Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile | Leu | Pro | Gln | Gln | |
| 305 | | | | 310 | | | | | | 315 | | | | | 320 | |
| Tyr | Leu | Arg | Pro | Val | Glu | Asp | Val | Ala | Thr | Ser | Gln | Asp | Asp | Cys | Tyr | |
| | | | 325 | | | | | 330 | | | | | | 335 | | |
| Lys | Phe | Ala | Ile | Ser | Gln | Ser | Ser | Thr | Gly | Thr | Val | Met | Gly | Ala | Val | |
| | | 340 | | | | | | 345 | | | | | 350 | | | |
| Ile | Met | Glu | Gly | Phe | Tyr | Val | Val | Phe | Asp | Arg | Ala | Arg | Lys | Arg | Ile | |

| | | | | |
|---|-----|-----|-----|-----|
| 130 | | 135 | | 140 |
| Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly | | | | |
| 145 | | 150 | | 155 |
| Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe | | | | 160 |
| | 165 | | 170 | |
| Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu | | | | 175 |
| | 180 | | 185 | |
| Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala | | | | 190 |
| | 195 | 200 | | 205 |
| Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr | | | | 210 |
| | 210 | 215 | | 220 |
| Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu | | | | 225 |
| | 230 | | 235 | |
| Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp | | | | 240 |
| | 245 | | 250 | |
| Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr | | | | 255 |
| | 260 | 265 | | 270 |
| Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile | | | | 275 |
| | 275 | 280 | | 285 |
| Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly | | | | 290 |
| | 290 | 295 | | 300 |
| Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe | | | | 305 |
| | 310 | | 315 | |
| Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe | | | | 320 |
| | 325 | | 330 | |
| Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val | | | | 335 |
| | 340 | | 345 | |
| Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser | | | | 350 |
| | 355 | 360 | | 365 |
| Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val | | | | 370 |
| | 375 | | 380 | |
| Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His | | | | 385 |
| | 390 | | 395 | |
| Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr | | | | 400 |
| | 405 | | 410 | |
| Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu | | | | 415 |
| | 420 | 425 | | 430 |

<210> 75

<211> 361

<212> PRT

<213> Homo sapiens

<400> 75

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| Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu | | | | |
| 1 | 5 | | 10 | 15 |
| Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr | | | | |
| | 20 | | 25 | 30 |
| Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His | | | | |
| | 35 | 40 | | 45 |
| Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys | | | | |
| | 50 | 55 | | 60 |
| Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly | | | | 65 |
| | 70 | | 75 | 80 |
| Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala | | | | |
| | 85 | 90 | | 95 |
| Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser | | | | |
| | 100 | 105 | | 110 |
| Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro | | | | |
| | 115 | 120 | | 125 |
| Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His | | | | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 130 | | 135 | | 140 | | | | | | | | | | | |
| Val | Pro | Asn | Leu | Phe | Ser | Leu | Gln | Leu | Cys | Gly | Ala | Gly | Phe | Pro | Leu |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |
| Asn | Gln | Ser | Glu | Val | Leu | Ala | Ser | Val | Gly | Gly | Ser | Met | Ile | Ile | Gly |
| | | | 165 | | | | | | 170 | | | | | | 175 |
| Gly | Ile | Asp | His | Ser | Leu | Tyr | Thr | Gly | Ser | Leu | Trp | Tyr | Thr | Pro | Ile |
| | | | 180 | | | | | 185 | | | | | | 190 | |
| Arg | Arg | Glu | Trp | Tyr | Tyr | Glu | Val | Ile | Ile | Val | Arg | Val | Glu | Ile | Asn |
| | | 195 | | | | 200 | | | | | | 205 | | | |
| Gly | Gln | Asp | Leu | Lys | Met | Asp | Cys | Lys | Glu | Tyr | Asn | Tyr | Asp | Lys | Ser |
| | 210 | | | | | 215 | | | | | | 220 | | | |
| Ile | Val | Asp | Ser | Gly | Thr | Thr | Asn | Leu | Arg | Leu | Pro | Lys | Lys | Val | Phe |
| 225 | | | | | 230 | | | | | 235 | | | | | 240 |
| Glu | Ala | Ala | Val | Lys | Ser | Ile | Lys | Ala | Ala | Ser | Ser | Thr | Glu | Lys | Phe |
| | | | 245 | | | | | 250 | | | | | | 255 | |
| Pro | Asp | Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val | Cys | Trp | Gln | Ala | Gly |
| | | | 260 | | | | | 265 | | | | | 270 | | |
| Thr | Thr | Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser | Leu | Tyr | Leu | Met | Gly |
| | 275 | | | | | | 280 | | | | | | 285 | | |
| Glu | Val | Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile | Leu | Pro | Gln | Gln | Tyr |
| | 290 | | | | | 295 | | | | | 300 | | | | |
| Leu | Arg | Pro | Val | Glu | Asp | Val | Ala | Thr | Ser | Gln | Asp | Asp | Cys | Tyr | Lys |
| 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| Phe | Ala | Ile | Ser | Gln | Ser | Ser | Thr | Gly | Thr | Val | Met | Gly | Ala | Val | Ile |
| | | | 325 | | | | | 330 | | | | | | 335 | |
| Met | Glu | Gly | Phe | Tyr | Val | Val | Phe | Asp | Arg | Ala | Arg | Lys | Arg | Ile | Gly |
| | | | 340 | | | | | 345 | | | | | 350 | | |
| Phe | Ala | Val | Ser | Ala | Cys | His | Val | His | | | | | | | |
| | 355 | | | | | 360 | | | | | | | | | |

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 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (1)...(63)
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 aay

60
 63

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 1 5 10 15
 Glu Met Val Asp Asn
 20

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<223> Peptide inhibitor P3-P4' XD-V

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<223> Xaa is hydroxyethylene or statine

<400> 78

Val Met Xaa Val Ala Glu Phe

1

5

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<211> 11

<212> PRT

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<400> 79

Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val

1

5

10

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<211> 419

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<213> Artificial Sequence

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<223> nucleotide insert in vector pCF

<400> 80

| | | | | | | |
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| aaccgcgtcgg | cctccgaacg | gtactccgcc | accgagggac | ctgagcgagt | ccgcatcgac | 120 |
| cggatcgga | aacctctcga | ctggttggggt | gagtactccc | tctcaaaagc | gggcatgact | 180 |
| tctgcgctaa | gattgtcagt | ttccaaaaaac | gaggaggatt | tgatattcac | ctggcccgcg | 240 |
| gtgatgcctt | tgagggtggc | cgcgtccatc | tggtcagaaa | agacaatctt | tttgttgtca | 300 |
| agcttgagggt | gtggcaggct | tgagatctgg | ccatacactt | gagtgacaat | gacatccact | 360 |
| ttgcctttct | ctccacaggt | gtccactccc | aggtccaact | gcaggtcgac | tctagaccc | 419 |

<210> 81

<211> 8

<212> PRT

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<220>

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<223> Xaa is hydroxyethylene or statine

<400> 81

Glu Val Met Xaa Val Ala Glu Phe

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<211> 9

<212> PRT

<213> Homo sapiens

<220>

<223> APP fragment P5-P4' wt

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 <211> 9
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<220>

<223> APP fragment P5-P4'wt

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 1 5

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 <211> 9
 <212> PRT
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<220>

<223> APP fragment

<400> 84
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 1 5

<210> 85
 <211> 9
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<400> 85
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 1 5

<210> 86
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 <400> 87
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 1 5

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 Ser Glu Val Asn Leu Ala Ala Glu Phe
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 1 5

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 <210> 95
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 <210> 96
 <211> 9
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 <400> 96
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 <210> 97
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1 5 10

<210> 98
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35

<210> 99
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<210> 101
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<220>
<223> Recombinant 293T cells

<400> 101
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1 5

<210> 102
<211> 10
<212> PRT
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<220>
<223> Recombinant CosA2 cells

<400> 102
Gly Ser Phe Val Glu Met Val Asp Asn Leu
1 5 10

<210> 103
<211> 4
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<213> Artificial Sequence

<220>

<223> APP substrate fragment:WT Sequence

<400> 103

Val Lys Met Asp

1

<210> 104

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> APP substrate fragment:Swedish Sequence

<400> 104

Val Asn Leu Asp

1

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